REMARKS

Entry of the foregoing and reexamination and reconsideration of the subject application as amended, pursuant to and consistent with 37 C.F.R. §1.112, are respectfully requested in light of the following remarks.

Status

As is correctly reflected in the Official Action, claims 1, 6-13 and 31-38 were previously pending and stand rejected. Claims 36 and 37 are amended above and Claims 39-41 are newly added.

Summary of Amendments

Claims 36 and 37 have been amended to simply require that said at least one enzyme and said at least one precursor are separated from each other. This is supported by at least page 1 of the specification, lines 15-20; page 2, line 25 to page 3, line 4 (which clearly indicates separation in what can be any form prior to contact just before or at the time of application) and page 4, line 1-9 (which disclose separation by packaging or by use of encapsulation and/or liposomes or microcapsules or microgranules) as well as by the Examples.

New Claims 39-41 parallel Claims 36-38, but specify that said at least one enzyme and/or at least one precursor are in encapsulated form and/or is/are included in liposomes or microcapsules or microgranules so as to separate them until the time of application. The support for this language is included in the sections of the specification noted above.

In light of the foregoing, it is clear that claims 36-41 do not introduce new matter into the application.

Rejection under 35 U.S.C. § 112, first paragraph:

Claims 36-38 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Applicants submit that this rejection cannot be maintained against these claims as amended or against new claims 39-41. The language of claims 36-38 now does not specify that the medium maintains the components separate but rather that the components are separated until application, which is clearly taught by the specification as already pointed out above. New claims 39-41 specify specific ways in which the components are separated other than by packaging, all of which are likewise supported by the as-filed written description. Withdrawal of the § 112 rejection is therefore in order and is earnestly solicited.

Rejection under 35 U.S.C. §103(a) – Boussouira et al. in view of Wheeler et al. and/or Berry et al.

Claims 1, 6-13, and 31-38 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent No. 6,153,205 to Boussouira et al. ("Boussouira et al.") in view of "*The biosynthetic pathway of vitamin C in higher plants*," by Glen L. Wheeler *et al.* ("Wheeler et al.") and/or U.S. Patent Application Publication No. 2002/0012979 A1 to Berry *et al.* ("Berry et al."). *See Official Action, Pages 3-7.* This rejection is respectfully traversed. Applicants submit that all claims now in this application are free of this rejection

Before reaching the merits of the pending rejection, Applicants wish to stress that when applying 35 U.S.C. § 103, four tenets of patent law must be adhered to: (1) the claimed invention must be considered as a whole, (2) the references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination, (3) the references must be viewed without the benefit of

impermissible hindsight vision, and (4) one of ordinary skill must have a reasonable expectation of success. *See M.P.E.P.* § *2141*, citing *Hodosh v. Block Drug Co., Inc.*, 786 F.2d 1136, 1143 (Fed. Cir. 1986). To establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation to modify the reference or to combine reference teachings, (2) there must be a reasonable expectation of success, and (3) the prior art reference(s) must teach or suggest all of the claim limitations. *See M.P.E.P.* § *2142; see also SIBIA Neurosciences, Inc. v. Cadus Pharm. Corp.*, 225 F.3d 1349, 1356 (Fed. Cir. 2000), which explains that if a reference needs to be modified to achieve the claimed invention, "there must be a showing of a suggestion or motivation to modify the teachings of that reference to the claimed invention in order to support the obviousness conclusion."

Applicants respectfully maintain that a *prima facie* case of obviousness has not been made out.

Applicants' Claimed Invention

In deciding whether a *prima facie* case of obviousness has been made out, it is important to keep in mind what Applicants have claimed. In the instant application, Applicants claim not simply ascorbic acid, but *topical compositions* comprising: (1) at least one ascorbic acid precursor that is *not* an ascorbic acid ester and that *is* L-galactono-1,4-lactone, L-gulono-1,4-lactone, D-glucorono-1,4-lactone, D-glucoronic acid, D-mannose, D-galacturonic acid, D-glucose, D-galactose, L-galactose, or mixtures thereof; (2) at least one enzyme that converts said ascorbic acid precursor to ascorbic acid; and (3) a cosmetically and/or dermatologically acceptable medium, with the enzyme and precursor each being present in a quantity

of 0.1% to 10% by weight; see independent claim 1. Independent claim 6 further requires that the enzyme is selected from the group consisting of L-galactono-1,4-lactone dehydrogenase, L-galactose dehydrogenase, L-sorbosone dehydrogenase, L-gulono-1,4-lactone oxidase, and mixtures thereof. Independent claims 9 and 31 parallel claims 1 and 6, respectively, but require that the enzyme and precursor be packaged separately. Independent claims 36 and 37 also parallel claims 1 and 6, respectively, but further require that the enzyme and the precursor are separated from each other until the time of application. Independent claims 39 and 40 likewise parallel claims 1 and 6, but require the enzyme(s) and/or precursor(s) is/are in encapsulated form and/or is/are included in liposomes or microcapsules or microgranules so as to separate them from each other until the time of application.

Boussouira et al.

The foundation for the Examiner's § 103(a) rejection is Boussouira et al. Boussouira et al., like Applicants, explain that while ascorbic acid, Vitamin C, has many beneficial attributes (*see, e.g., Boussouira et al. Column 1, Lines 19-24*), it is unstable and sensitive to external factors such as light and heat. *See Boussouira et al. Column 1, Lines 36-38*. Unfortunately, "[t]his instability goes against the desired efficacy and, what is more, can be the source of unpleasant sensations for the user, for example when the instability of the active agent leads to changes in the color and/or odor of the composition containing it." *Boussouira et al. Column 1, Lines 38-42*. Boussouira et al. then explain that several solutions have been proposed for stabilizing active ingredients such as Vitamin C, but those solutions have presented other difficulties, such as a decrease in efficacy and prevention of rapid release of Vitamin C in sufficient quantity. *See*

Boussouira et al. Column 1, Lines 49-59. Boussouira et al. conclude that there is "a need for a topical application product containing vitamins used in cosmetics and/or dermatology, in which these vitamins conserve all their properties and thus their efficacy over time." *Boussouira et al. Column 1, Lines 60-63.*

According to Boussouira et al., EP 710,478 satisfies that need by using lipase with esters of Vitamin C. *See Boussouira et al. Column 1, Lines 64-67.* Boussouira et al. then announce that they have discovered another way to satisfy that need by introducing C_6 to C_{22} alcohols into compositions having lipase and Vitamin C esters. *See Boussouira et al. Column 2, Lines 1-4.* Boussouira et al.'s solution to the foregoing Vitamin C problem is to ensure that their products have: (1) a lipase; (2) at least one precursor of a vitamin wherein the precursor is an ester with a linear or branched, saturated or unsaturated chain containing 2 to 25 carbon atoms; (3) at least one C_6 to C_{22} alcohol; and (4) a ratio of alcohol to precursor of 0.25 to 30/1. *See, e.g., Boussouira et al. Claim 1*; Abstract; Column 2, lines 8-13; Column 2, lines 66 to column 3, line 40.

It is respectfully submitted that the Examiner has mischaracterized the Boussouira et al. patent, and by doing so has made the reference appear to be more relevant than it actually is. The Boussouira et al. patent does not disclose a broad class of vitamin precursors and then specifically identify a particular type of precursor, the esters. The Examiner states on page 6 of the Action that Boussouira et al. do not teach that the esters are the only precursors that could be used. This statement is clearly in error, and it is upon this erroneous statement that the Examiner has built a house of cards, that is, it is the basis for obviousness rejection. Without this basis, the rejection must fall.

The fact is that the Boussouira et al. patent discloses esters, and indeed, only particular sorts of esters, as vitamin precursors for use in their invention. In the Summary of the Invention, Column 2, lines 7-18, Boussouira et al. state that their topical product comprises, as one essential, "at least one precursor of a vitamin used in cosmetics and/or dermatology which is an ester comprising at least one ester function with a linear or branched, saturated or unsaturated chain containing from 2 to 25 carbon atoms". Thus, Boussouira et al. clearly teaches that they define precurors to mean alkyl or alkenyl esters. They state that their precursors are esters, only esters. Boussouira et al. further state, beginning in Column 2, line 66:

> As used herein, the term "precursor of a vitamin" refers to a esterified vitamin which is hydrolyzed on the skin to produce the free vitamin.

Thus, the patent's use of the term "precursor" is limited to esters. Boussouira et al. go on to describe further the characteristics of the esters in their composition. Nowhere is there a suggestion that their vitamin precursors can be anything other than esters.

Applicants emphasize that Boussouira et al. require that their vitamin precursors are esters and that those esters be hydrolyzed on the skin to produce the free vitamin. Boussouira et al. describe as another essential ingredient of their composition "at least one enzyme which is a lipase" (Column 2, lines 8-9). Boussouira et al. further provide a definition of a lipase in Column 2, lines 40-43:

> A lipase is an enzyme which is known to hydrolyze triglycerides into mono- and diglycerides, into glycerol and into free fatty acids.

Boussouira et al. neither disclose nor suggest that their vitamin precursor can be other than an ester or that their enzyme can be other than lipase, which is

an enzyme know to hydrolyze esters. Further, as noted above, they require that their ester be hydrolyzed on the skin. The fact that the words "precursor" and "enzyme" are capable of broader interpretations than "ester" and "lipase", respectively, does not mean that these terms can be interpreted broadly in the case of Boussouira et al. because Boussouira specifically define these terms narrowly and it is well-settled in patent law that Applicants can be their own lexigraphers. The Examiner is not allowed to interpret the patent's teaching more broadly when the patent clearly teaches narrower definitions of the terms in question.

All of applicants' claims require an ascorbic acid precursor which is not an ester and which is L-galactono-1,4-lactone, L-gulono-1,4-lactone, D-glucorono-1,4-lactone, D-glucoronic acid, D-mannose, D-galacturonic acid, D-glucose, D-galactose, L-galactose, or a mixture thereof. Not one of these precursors is an ester. Boussouira et al. neither describe nor suggest any ascorbic acid precursors which are not esters, much less the particular precursors named in applicants' claims.

Applicants' claim 6 and its dependent claims and claim 37 and its dependent claim and claim 40 and its dependent claim further specify that the enzyme is L-galactono-1,4-lactone dehydrogenase,
L-galactose dehydrogenase, L-sorbosone dehydrogenase or L-gulono-1,4-lactone oxidase or a mixture thereof. None of these is a lipase, as absolutely required by Boussouira et al.; none of these hydrolyze applicants' precursors, which is the reaction essential in Boussouira et al.'s invention.

There is no motivation to modify and combine Boussouira et al. with Wheeler et al. or Berry et al. because Boussouira et al. teach away from Applicants' invention

As explained above, to establish a *prima facie* case of obviousness, there must be some suggestion or motivation to modify the reference or to combine reference teachings. To arrive at Applicants' invention using Boussouira et al., one must modify **completely** Boussouira et al.'s requirement that the composition contain a vitamin *ester*. Applicants' compositions specifically ***exclude*** esters. There is nothing in Boussouira et al. to suggest to or motivate one of skill in the art to disregard that which Boussouira et al. have emphasized as critical to the success of their compositions. That is, there is nothing in Boussouira et al. that suggests or motivates one of skill to exclude the vitamin ester and insert in its stead a substance which cannot be hydrolyzed to the vitamin.

The Examiner has stated that "Boussouira clearly teaches compositions of ascorbic acid precursors, in combination with enzymes will effectively produce the active vitamin (col. 2 line 41 – col. 3 line 1)." *See Official Action, Page 6.* This statement misrepresents the very section of the reference which clearly teaches quite the opposite, i.e., that the reference's precursors must be esters which are hydrolyzed on the skin to release the vitamin. Applicants' precursors are not esters and are not hydrolyzed on the skin to release the vitamin. Not only do Boussouira et al. fail to suggest to or motivate one to modify its ester precursor attribute, it teaches away from doing so by emphasizing the beneficial combination of lipase, ester vitamin precursor, C_6 to C_{22} alcohol, and alcohol to precursor ratio.

Moreover, ascorbic acid may be produced according to several pathways. Boussouira et al. rely upon the fact that ascorbic acid esters are naturally hydrolyzed by esterases, whereas Applicants' invention relies upon a synthesis mechanism involving sugars and oxidizing enzymes. Nothing in Boussouira et al. suggests to or motivates one to pursue a combination which makes use of a totally different

pathway, especially in light of Boussouira et al.'s claim that only they and EP 710,478 (which shares the lipase plus ester combination) overcome past difficulties with active ingredients such as Vitamin C, and in light of Boussouira et al.'s requirement that their ester be hydrolyzed by lipase. Applicants' precursors are sugars, not esters, and their enzymes are specific dehydrogenases and oxidases which convert the sugars to ascorbic acid by oxidation, not by hydrolysis.

Neither Wheeler et al. nor Berry et al. cure Boussouira et al.'s deficiencies

Even if one of skill in the art were somehow prompted prior to Applicants' invention to disregard the ester precursor mandate, the lipase mandate and the hydrolysis mandate of Boussouira et al. which is not justified by Boussouira et al. Applicants maintain that the ordinary skilled person would not have looked to either Wheeler et al. or Berry et al. for guidance.

The Boussouira et al. patent is directed to topically-applicable compositions and methods for making such compositions containing a lipase, an ester vitamin precursor, a fatty alcohol, and a particular alcohol to precursor ratio. Wheeler et al. is directed not to compositions, let alone topically-applicable vitamin precursor ester/lipase/fatty alcohol compositions, but to a proposed pathway for ascorbate biosynthesis in higher plants. *See Wheeler et al., Page 368, & 2.* As a result of the experiments conducted and the conclusions drawn therefrom, Wheeler et al. conclude only that "[w]e are now in a position to investigate the subcellular localization and control of ***ascorbate*** biosynthesis in ***plants*** and, ultimately, to manipulate its content with ***potential benefits*** for human nutrition and plant resistance to oxidative stress." *Wheeler et al., Page 368, & 4* (emphasis added). This is at most an invitation to experiment with ascorbate biosynthesis in plants to

obtain some benefits for human nutrition. However, as the Examiner is well aware, such is not a proper basis for an obviousness rejection. And, of course, this invitation teaches nothing relevant to a totally different pathway to ascorbic acid and its use by Boussouira et al.

Applicants stress that the fact that Wheeler et al. happen to disclose that "ascorbic acid precursors 1-galactose and 1-galactono-1,4-lactone are converted to ascorbic acid by 1-galactose dehydrogenase" is of no moment. *See Official Action, Page 4.* Mere identification of each claimed element in the prior art is NOT sufficient to negate patentability. *In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998). Instead, there "must be a teaching or suggestion within the prior art, or within the general knowledge of a person of ordinary skill in the field of the invention, to look to particular sources of information, to select particular elements, and to combine them in the way they were combined by the inventor." *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534, 536 (Fed. Cir. 1998). Otherwise, sophisticated scientific fields would rarely, if ever, experience a patentable technical advance. *Rouffet*, 149 F.3d at 1357.

Similarly, the Berry et al. patent publication is as far afield from Boussouira et al. as is the Wheeler et al. reference. The Berry et al. publication relates not to compositions, let alone topically-applicable vitamin precursor ester/lipase/fatty alcohol compositions, but to methods for producing Vitamin C and esters thereof in microorganisms, genetically-modified microorganisms for producing Vitamin C and esters thereof, and to genetically modified plants for producing Vitamin C and esters thereof. *See, e.g., Berry et al. Claims 1-72.* Berry et al. appear to have beneficially modified ascorbate biosynthesis in plants, which Wheeler et al. posited as a possible use of their theory of ascorbic acid biosynthesis. Applicants disagree that one of skill

in the art would look to information on *genetically-modified microorganisms* for guidance herein.

Applicants respectfully reiterate that a *prima facie* case of obviousness has not been made out. Where is the crucial motivation or suggestion to combine the cited references? Indeed, it does not exist, except in the Examiner's mind. There is simply no motivation or suggestion in the art to combine and modify Boussouira et al., Wheeler et al., and/or Berry et al. as suggested by the Examiner.

With all due respect, it is submitted that is only a 20-20 hindsight interpretation of the references, coupled with an actual misunderstanding of what is taught by the primary Boussouira et al. reference, using applicants' own teachings as a guide through the maze of the prior art, which can lead to the present rejection. This is not a proper basis for a 35 U.S.C. §103 rejection.

In light of the foregoing, Applicants respectfully request withdrawal of the 35 U.S.C. § 103(a) rejection of Claims 1, 6-13, and 31-38 over Boussouira et al. in view of Wheeler et al. and/or Berry et al. and allowance of all of the claims now in this application.

CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions relating to this response, or the application in general, it would be greatly appreciated if the Examiner would telephone the undersigned agent concerning such questions so that the prosecution of this application may be expedited.

Respectfully submitted,

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